Obstructive Sleep Apnea, Hypoxia, and Metabolic Syndrome in Psychiatric and Nonpsychiatric Settings

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ABSTRACT

Obesity continues to be a serious cause of morbidity and mortality globally and particularly in North America. Primary manifestations of obesity include obstructive sleep apnea (OSA) and depression associated with a decrease in immune defense mechanisms, possibly related to increased cytokine levels. Secondary manisfestations of obesity possibly result from a cascade of events and include insulin resistance/hyperglycemia, hyperlipidemia, and hypertension—all of which comprise metabolic syndrome. This paper reviews sleep disturbances in general and OSA in psychiatric patients, particularly those who are obese.

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BACKGROUND

Although sleep disturbance is a common symptom of major depression, it is frequently under-recognized, particularly in psychiatric patient samples.[1] Although it is clear that normalizing the architecture of sleep is predictive of depression treatment,[2] the incidence of obstructive sleep apnea (OSA) in the psychiatric population appears to be rising. As an entity, OSA appears to occur more commonly in neuropsychiatric conditions than with other medical conditions.[3,4] This risk appears to be bidirectional, with obesity contributing to airway obstruction during sleep and psychiatric illness and its treatment being associated with weight gain.[5] Exploring the association between psychiatric illnesses, obesity, and OSA could help define the treatment strategies relevant to individual cases as opposed to generic treatment directed toward symptom relief.

PRIMARY MANIFESTATION/ OBSTRUCTIVE SLEEP APNEA

OSA is the most common breathing-related sleep disorder, making up 40 to 50 percent of sleep disorder diagnoses. By definition, OSA is a cluster of frequent breathless episodes (apneic) lasting seconds to minutes during sleep as a result of airway obstruction. Sleep

apnea is divided into central and obstructive types, the latter of which is more common. Central sleep apnea tends to occur more commonly in combination with OSA and can be seen sometimes without weight gain. These apneic episodes are classified into obstructive, mixed, or hypopneic.

Depending on the frequency (measured by apnea/hypopnea index or AHI) and severity of these episodes (denoted by a significant drop in blood-oxygen saturation levels measured by respiratory distress index or RDI), wakefulness and frequent sleep interruptions occur. Insomnia, as a result, manifests as trouble staying asleep, restlessness, and lack of restorative sleep leaving the person tired and sleep deprived the following day. The resulting excessive daytime sleepiness limits the person's functional ability, frequently causing car accidents and decreasing quality of life.[6] Snoring, a sign of distress resulting from obstruction of the airway, is most commonly experienced with OSA and observed by the spouse. Snoring is normally absent in central apnea and aids in distinguishing between the two types of apneas.

The prevalence of OSA is as high as 1 in 12 (4.4%) Americans, with about 1 in 27 (3.68%) of the population having undiagnosed OSA. The risks and costs of undiagnosed or untreated OSA could be staggering with some recent estimates putting it at $11.1 billion per year in indirect costs (e.g, motor vehicle accidents) and $3.1 billion in direct costs for screening and treating the disorder.[6,7]

SECONDARY MANIFESTATION/ METABOLIC SYNDROME

OSA can progress with associated hypoxia hypothetically transforming into metabolic syndrome leading to end organ damage, i.e., myocardial infarction and cerebral vascular accidents.[8]

Metabolic syndrome, in our opinion, is a later/secondary complication of continued obesity with a body mass index (BMI) over 30 triggering insulin resistance/hyperglycemia,[9] hyperlipidemia, and hypertension. Metabolic syndrome was observed in 51 percent of psychiatric outpatients screened during one day in a recent study.[10] This number is substantially higher than the 42 percent previously reported by the National Institutes of Health-sponsored Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study.[11] In addition, the Hordaland Health Study[12] demonstrated a strong association between the use of selective serotonin reuptake inhibitors (SSRIs) and metabolic syndrome.

Metabolic syndrome is a growing concern globally and is rising across all age groups in the general population.[13,14] Also, the prevalence of metabolic syndrome appears to increase with the age of the population according to independent observations.[15]

DISCUSSION

The prevalence of metabolic syndrome appears to be much higher than OSA (25% vs. 4.1%, respectively). In one study, the prevalence of metabolic syndrome in patients suffering from OSA[16] was 60 percent versus 40 percent in those who did not have metabolic syndrome; this latter segment potentially represents age-related cardiac complications, such as hypertension. This also raises the possible involvement of other sleep-related disorders associated with depression, such as reduced slow wave sleep (SWS),[17] disinhibition of REM sleep (shortening of REM latency, prolongation of the first REM period, increased REM density) and chronic sleep loss or sleep fragmentation[18] associated with restricted sleep endemic in modern society—all of which may lead to changes in insulin sensitivity prior to developing OSA via neuroendocrine mechanisms as demonstrated experimentally.

If this literature is considered relevant, then an important preventive measure for metabolic syndrome might include proper screening for OSA in outpatient psychiatric and general medical settings, especially in patients with hypothyroidism. The need was further substantiated by another study evaluating the pre-test probability of OSA. This study had a 78-percent return rate from 8,000 surveys conducted across all age groups in primary care settings.[19] OSA is clearly underdiagnosed or at least poorly reported by some specialty groups (e.g., cardiology) due to lack of confidence according to one survey.[20] The addition of screening all patients at risk for OSA during pre-registration health checks in outpatient settings, although possible, would be cumbersome.[21] However, a brief, simple screening tool might increase the cost effectiveness of conducting such assessments.

SUMMARY

In summary, chronic sleep loss, whether behavioral or sleep-disorder related, may represent a novel risk factor for weight gain, insulin resistance, and type 2 diabetes. Therefore, we propose the development of a concise sleep apnea scale (SAS) geared toward sleep-related disorders in outpatient settings.

After assessing and ruling out other sleep disorders as a first step, evaluating for OSA symptoms (e.g., snoring, choking, and increased daytime sleepiness) and noting psychotropic and other medication use, weight gain, and other comorbidities, many patients with OSA could be prospectively identified. Based on the results of the screening assessment, polysomnography should be considered to confirm OSA as well as other sleep disorders.

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